

## Evaluation of Gastrointestinal System Findings in Crimean-Congo Hemorrhagic Fever Patients

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### Abstract

**Aim:** Crimean-Congo hemorrhagic fever (CCHF) is a disease caused by a virus. Early diagnosis of CCHF particularly in regions where the disease frequently occurs is important for taking necessary measures and for immediately starting the treatment process. This study aims to evaluate gastrointestinal system (GIS) findings in the patients.

**Materials and Methods:** Patient history, such as nausea, vomiting, abdominal pain, diarrhea, values of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, and contact with tick, was recorded. Enzyme-linked immunosorbent assay and/or Polymerase Chain Reaction tests were used for diagnoses.

**Results:** The ratio of tick bite history was found to be 73.1%. According to the GIS findings of the patients at the time of admission, the ratio of nausea and vomiting, abdominal pain, diarrhea, and elevated AST and ALT levels were 61.2%, 37.6%, 27.9%, and 78.4% respectively. Five of the 93 patients died, and the mortality rate was 5.4%.

**Conclusion:** Considering that early diagnosis is vital for the clinical course of the patients and the prevention of hospital infections and that every patient may not have a history of tick bite, it should be kept in mind that the disease can occur particularly with GIS findings in high season living in endemic regions and thus CCHF should be suspected. (*Eurasian J Emerg Med* 2016; 15: 105-7)

**Keywords:** Crimean-Congo Hemorrhagic Fever, gastrointestinal findings, tick, viral hemorrhagic fever

### Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a disease caused by a virus of the Bunyaviridae family and has been reported in Asia, Africa, the Middle East, and Eastern European regions, as well as has been observed in Turkey since 2002. Early diagnosis of the disease, particularly in regions where it frequently occurs, is important for taking isolation measures and for immediately starting the treatment process (1).

The infection can be transmitted by contact with a CCHF-infected person, infected ticks, and farm animals. It clinically presents with a dramatic progress characterized by diffused hemorrhages, weakness, and fever. Liver enzymes, creatinine phosphokinase, and lactate dehydrogenase levels of these patients are elevated, and an endothelium infection plays a profound pathogenic role (2).

Crimean-Congo hemorrhagic fever, which is transmitted by ticks, is noteworthy because of its increasing prevalence and resulting mortality, particularly in recent years. Early diagnosis is important for a better clinical course of the patient and for the prevention of hospital infections. Management of patients is based on supportive care (3, 4).

Laboratory diagnosis of CCHF is made by identifying viral nucleic acids using a real-time reverse transcriptase polymerase chain reaction (PCR) or by identifying IgM positive or IgG seroconversion using enzyme-linked immunosorbent assay (ELISA) in blood or body fluid samples (5).

The symptoms occur because of the direct effect of the virus on target organs. Immunohistochemical analyses have shown the presence of intense antigens in the endothelium and liver. Symptoms in the early period of the disease are non-specific and can be confused with various manifestations. Nausea, vomiting, abdominal pain, and short-term diarrhea can occur in the early stage of the disease. Hypovolemia, hypoxia, and shock can develop in patients who have simultaneous hemorrhage from various regions, particularly in the gastrointestinal system (GIS) (6). In this study, we aimed to evaluate GIS findings in CCHF patients at the time of admission to the hospital.

### Materials and Methods

We retrospectively evaluated 93 patients in Artvin who were diagnosed with CCHF in the period from January 2011 to April 2014, using

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computer records of the patients. Patients' history of nausea, vomiting, abdominal pain, diarrhea, aspartate aminotransferase (AST), alanine aminotransferase (ALT) elevation levels, and contact with ticks were recorded from the national case report form of CCHF. Because the patients' data were obtained from the National CCHF form, numerical data could not be obtained; GIS findings of the patients in this system are not reported in numerical values but instead are recorded as "yes/no."

ELISA and/or PCR tests were performed to diagnose the patients from blood samples analyzed by a reference laboratory. ELISA was used to determine CCHF virus Immunoglobulin IgM antibody positivity and Real-Time PCR was used to determine the presence of CCHF viral RNA. Data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 15. Results were reported as a numerical value, percentage, and mean.

## Results

The study included a total of 93 patients with CCHF in the emergency service of Artvin Government Hospital. The demographic characteristics of the patients were as follows: 50 were men and 43 were women; mean age was  $44.8 \pm 10.8$  years. The proportion of patients with tick bite history was 73.1%. According to the GIS findings of the patients at the time of admission, 61.2% had nausea and vomiting, 37.6% had abdominal pain, 27.9% had diarrhea, and 78.4% had elevated AST and ALT levels. Five of the 93 patients with CCHF died, and the mortality rate was 5.4% (Table 1).

## Discussion

Crimean-Congo hemorrhagic fever disease is characterized by signs and symptoms like fever, nausea, vomiting, headache, myalgia, elevated liver enzymes, and mucocutaneous hemorrhage, as well as life-threatening intravenous coagulation and massive hemorrhages

(7). GIS findings of CCHF patients from some previous studies are presented for comparison in Table 2 (8-19, 21, 22).

Crimean-Congo hemorrhagic fever is more common in people of the working age dealing with agriculture and animal husbandry who are more exposed to tick bites than other members of the population (4). In our study, 75% of the patients were found to have a history of tick bites. This proportion ranged between 50% and 82% in previous studies (8, 9, 11-16, 18, 19).

In our study, levels of nausea and vomiting rose to 80% and elevated AST and ALT to 100% in patients who died from CCHF. We detected a significantly higher proportion of nausea and vomiting in the deceased patients than in the survivors. Bakir et al. (13) reported significantly higher AST levels in deceased patients in their study. Ergonul et al. (14) observed that the proportions of melena, hematemesis, and nausea and vomiting were 100% in deceased patients. Hatipoglu et

**Table 1.** Evaluation of GIS findings of the patients with CCHF

	Survivors (n=88)	Death (n=5)	Total (n=93) n (%)
Age mean±SD	41.1±15.7	38.9±15.1	40.8±10.8
Male/Female	47/41	3 / 2	50/43
Tick bite history	63	5	68 (73.1)
Nausea and vomiting	53	4	57 (61.2)
Abdominal pain	33	2	35 (37.6)
Diarrhea	25	1	26 (27.9)
Elevated AST, ALT	68	5	73 (78.4)

GIS: Gastrointestinal System; CCHF: Crimean-Congo Hemorrhagic Fever; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase

**Table 2.** The percentages of GIS findings of CCHF patients from previous studies

Study	Nausea	Vomiting	Diarrhea	Abdominal Pain	Elevated AST/ALT	Hematemesis	Melena	HM	Number of Cases
Gonen (8)	40	40	20	40	60	6			15
Ozturk et al. (9)	70	45	35	25				5	20
Karti et al. (10)	84	84	37	84				21	19
Ertugrul et al. (11)	69	46	35	42	77				25
Cevik et al. (12)	51	51	20			13	17	19	69
Bakir et al. (13)	75	68	33			8	1	30	92
Ergonul et al. (14)	83	83	35			31	20	35	54
Ergonul et al. (16)	80	80	31			29	17	37	35
Belet et al. (17)	39	59	22	22	61/29				54
Tuygun et al. (18)	60	60							50
Yilmaz et al. (19)	65	43	25	33	86				1820
Schwarz et al. (21)	64		46						11
Kadanali et al. (22)	60	48	19					20	63
Present study	61.2	61.2	27.9	37.6	78.4				93

HM: Hepatosplenomegaly; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase

al. (20) reported that the proportion of diarrhea and ALT and AST values of the deceased patients were higher than of those who survived. Kadanali et al. (22) similarly found a vomiting proportion of 100% and found that AST and ALT levels were higher in the deceased patients than in those who survived.

A literature review from Turkey revealed a CCHF patient who was admitted to the hospital with a clinical presentation mimicking acute appendicitis, another patient who was admitted with abdominal pain and hematemesis, and another one who was admitted because of elevated transaminase (23, 24). Similarly, the literature contains a case presentation involving a patient who was admitted to hospital because of abdominal pain and died within 24 h (25). In a study carried out in India, it was reported that two patients were admitted to the hospital for abdominal pain and vomiting (26). The proportion of abdominal pain was 37.6% in the patients of the present study.

In a study performed in Turkey that included 42 dyspeptic patients hospitalized because of CCHF, the patients were divided into two groups according to fecal *Helicobacter pylori* positivity and the clinical and laboratory acuteness criteria of CCHF; the study reported no difference between the two groups in terms of clinical and laboratory criteria (27).

## Conclusion

In our study, we observed the GIS findings of CCHF patients as 61.2% of the patients had nausea and vomiting, 37.6% had abdominal pain and 27.9% had diarrhea. Because not all patients had a history of tick bite, it should be kept in mind that the disease can occur with GIS findings in the high season, particularly in people living in endemic regions; therefore, CCHF should be suspected.

**Ethics Committee Approval:** Ethics committee approval is not required because of our study was performed retrospectively.

**Informed Consent:** Written informed consent is not required because of our study was performed retrospectively.

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## References

1. Yilmaz GR, Buzgan T, Cevik MA, Safran A, Uzun R, Cevik MA, et al. The Evaluation of Knowledge of the Health-Care Personnel Regarding Crimean-Congo Haemorrhagic Fever. *Flora J* 2009; 4: 27-35.
2. Ergonul O. Crimean-Congo haemorrhagic fever. *Lancet Infect Dis* 2006; 6: 203-14. [CrossRef]
3. Kaygusuz S. Preliminary Study Indicating the Epidemiological Situation of the Ticks in Kırkkale-Kızılırmak Basin. *Kırkkale Uni J* 2008; 10: 1-4.
4. Ergonul O. Crimean-Congo Haemorrhagic Fever. *Ankem J* 2009; 23: 234-40.
5. Uyar Y, Carhan A, Albayrak N, Altaş AB. Evaluation of PCR and ELISA-IgM results in the laboratory diagnosis of Crimean-Congo haemorrhagic fever cases in 2008 in Turkey. *Microbiology J* 2010; 44: 57-64.
6. Ozkurt Z. Crimean-Congo haemorrhagic fever. *Intensive Care J* 2007; 7: 85-90.
7. Duru F, Fisgin T. Hematological aspects of Crimean-Congo hemorrhagic fever. *Turk J Hematol* 2009; 26: 161-6.
8. Gonen I. Clinical and laboratory findings of patients with Crimean-Congo hemorrhagic fever in the emergency department at hospital admission. *JMID* 2011; 1: 1-4. [CrossRef]
9. Ozturk DB, Kuscü F, Gurbuz Y, Gül S, Tütüncü EE, Şencan İ. Evaluation of 20 CCHF cases during 2006-2007 years. *Klimik J* 2008; 21: 93-6.
10. Karti SS, Odabasi Z, Korten V, Yılmaz M, Sonmez M, Caylan R, et al. Crimean-Congo hemorrhagic fever in Turkey. *Emerg Infect Dis* 2004; 10: 1379-84. [CrossRef]
11. Ertugrul B, Uyar Y, Yavas K, et al: An outbreak of Crimean-Congo hemorrhagic fever in western Anatolia, Turkey *International Journal of Infectious Diseases* 2009;13:431-436.
12. Ertugrul B, Uyar Y, Yavas K, Turan C, Oncu S, Saylak O, et al. Clinical and laboratory features of Crimean-Congo hemorrhagic fever: predictors of fatality. *Int J Infect Dis* 2008; 12: 374-9. [CrossRef]
13. Bakir M, Ugurlu M, Dokuzoguz B, Bodur H, Tasyaran MA, Vahaboglu H, et al. Crimean-Congo haemorrhagic fever outbreak in Middle Anatolia: a multicentre study of clinical features and outcome measures. *J Med Microbiol* 2005; 54: 385-9. [CrossRef]
14. Ergonul O, Celikbas A, Baykam N, Eren S, Dokuzoguz B. Analysis of risk-factors among patients with Crimean-Congo haemorrhagic fever virus infection: severity criteria revisited. *Clin Microbiol Infect* 2006; 12: 551-4. [CrossRef]
15. Midilli K, Gargili A, Ergonul O, Sengöz G, Ozturk R, Bakar M, et al. Imported Crimean-Congo hemorrhagic fever cases in Istanbul. *BMC Infect Dis* 2007; 7: 54. [CrossRef]
16. Ergönül O, Celikbaş A, Dokuzoguz B, Eren S, Baykam N, Esener H. Characteristics of patients with Crimean-Congo hemorrhagic fever in a recent outbreak in Turkey and impact of oral ribavirin therapy. *Clin Infect Dis* 2004; 39: 284-7. [CrossRef]
17. Belet N, Top A, Terzi O, Arslan HN, Baysal K, Sensoy G. Evaluation of children with Crimean-Congo hemorrhagic fever in the central Blacksea region. *Pediatr Infect Dis J* 2014; 33: e194-7.
18. Tuygun N, Tanir G, Caglayik DY, Uyar Y, Korukluoglu G, Cenesiz F. Pediatric cases of Crimean-Congo hemorrhagic fever in Turkey. *Pediatr Int* 2012; 54: 402-6. [CrossRef]
19. Yılmaz GR, Buzgan T, Irmak H, Safran A, Uzun R, Cevik MA, et al. The epidemiology of Crimean-Congo hemorrhagic fever in Turkey, 2002-2007. *Int J Infect Dis* 2009; 13: 380-6. [CrossRef]
20. Hatipoglu CA, Bulut C, Yetkin MA, Ertem GT, Erdinc FS, Kilic EK, et al. Evaluation of clinical and laboratory predictors of fatality in patients with Crimean-Congo haemorrhagic fever in a tertiary care hospital in Turkey. *Scand J Infect Dis* 2010; 42: 516-21. [CrossRef]
21. Schwarz TF, Nsanze H, Ameen AM. Clinical features of Crimean-Congo haemorrhagic fever in the United Arab Emirates. *Infection* 1997; 25: 364-7. [CrossRef]
22. Kadanali A, Ozden K, Erol S. Crimean-Congo Hemorrhagic Fever Virus Infection: Clinical and Laboratory Observations and Predictors of Fatality. *Turkiye Klinikleri J Med Sci* 2012; 32: 432-7. [CrossRef]
23. Celikbas A, Ergonul O, Dokuzoguz B, Eren S, Baykam N, Polat-Düzgün A. Crimean-Congo hemorrhagic infection simulating acute appendicitis. *J Infect* 2005; 50: 363-5. [CrossRef]
24. Gonen I, Ermis F. Crimean-Congo hemorrhagic fever presenting with gastrointestinal manifestations: two cases. *Turk J Gastroenterol* 2014; 25: 120-1. [CrossRef]
25. Saleem J, Usman M, Nadeem A, Sethi SA, Salman M. Crimean-Congo hemorrhagic fever: a first case from Abbottabad, Pakistan. *Int J Infect Dis* 2009; 13: e121-3.
26. Patel AK, Patel KK, Mehta M, Parikh TM, Toshniwal H, Patel K. First Crimean-Congo hemorrhagic fever outbreak in India. *J Assoc Physicians India* 2011; 59: 585-9.
27. Dokmetas I, Yonem O, Dokmetas S, Ozdemir L, Kilicli F, Engin A, et al. Effect of *H. pylori* presence on the severity of Crimean Congo hemorrhagic fever. *Endoscopy J* 2014; 22: 11-3.